STUDY OF ENDOMETRIAL GLYCOGEN IN CASES OF DYSFUNCTIONAL UTERINE HAEMORRHAGE & SUBFERTILITY

by

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The endometrium is one of the most dynamic structures in the human body characterised by a complete life cycle within a short span of time. The constantly changing structure of normal and abnormal endometrium is associated with fundamental biochemical alterations which can be studied histochemically. Glycogen and its products of metabolism are considered to be the most important and are believed to be the direct source of nutrient for the early conceptus from the time it enters the uterine cavity to the time it is actively supported by maternal blood stream. Failure of endomentrium to produce adequate amount of glycogen gives rise to "Glycopenic Uteri" (Zondek and Stein, 1940 and Zondek and Shapino, 1942) or poor quality endometrium (Hughes, 1950) resulting in the death of the ovum either before or after implantation. This will lead to sterility or habitual abortion. For this reason efforts have been directed towards studying abnormalities in endometrial glycogen with the hope that a cause for many cases of sterility, habitual abortion and functional uterine bleeding could be elicited.

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Material and Method

The present study was carried out in 225 patients attending out patients department of upper India Sugar Exchange Maternity Hosptal, Kanpur. Out of these 65 were of primary sterility, 25 of secondary sterility, 10 of habitual abortion, 100 of functional uterine bleeding and 25 were selected as control cases who had normal menstrual cycles and had two or more normal pregnancies without complications. Patients in sterility group, including their husbands, were investigated and all routine tests related to the problems of infertility were found to be normal and study of endomentrium was resorted to as an attempt to find the cause of these problems. Each patient was examined and excluded from the present study if any organic, systemic or pelvic disease was found. Endometrium was obtained in various phases of menstrual cycle by endometrial biopsy, diatation and curettage or from hysterectomy specimens removed for functional uterine bleeding.

All tissues were processed for routine histology and glycogen (Mc Manus, 1960). They were histologically dated

according to criteria of Noyes (1950). Histochemical reaction for glycogen was divided into following groups:

—	Negative	
+	Traces	Very small granules
++	Mild	Coarse granules
+++	Moderate	Small masses
++++	Marked	Large masses

Observations

Glycogen was found to follow a definite cyclical pattern. It was present in traces in early proliferative phase and appeared in basal portion of the epithelial cells in the form of small granules. It was seen to increase in amount in late proliferative phase and as cycle progressed it increased rapidly in early secretory phase. Glycogen was found to extend from its previous subnuclear position towards the luminal tips and ultimately into the lumina of glands. Cells showing predecidual reactions were strongly positive for glycogen. The endothelial cells lining the arterioles as well as the muscular tunic contained glycogen. The greatest amount of glycogen was found in early secretory phase.

Sterility Group

Histological data was related with the day of menstrual cycle whence tissue was obtained. In control group all the specimens corresponded to the phase in which tissue was obtained, but it was not so in sterility group. 11.00% proliferative endomentria were histologically immature (8.00% in primary sterility, 2.00% in secondary sterility and 1.00% in habitual abortion group). Similarly, 16.00% of progestational endometria showed histological retardation in secretory phase. Out of 11 immature endometria found in proliferative phase only 2 attained maturity in secretory phase and rest of them were found to be immature in secretory phase also (Table I).

Histochemical study

The general distribution of glycogen was on the same pattern as in normal specimens. Endometria obtained in early secretory phase showed glycogen deficiency in 14 (18.66%) specimens of primary sterility and 3 (10.72%) of secondary sterility and 2 of habitual abortion (16.67%). In 12 specimens of primary sterility, 4 of secondary sterility and 1 of habitual abortion group, there was no glycogen at all in early secretory phase. In late secretory phase glycogen deficiency (i.e. present in traces or none at all) was found in 9 specimens (10.58%), 5 in primary sterility and 2 each of secondary sterility and habitual abortion group respectively (Table II, III & IV).

TABLE I

Histological Maturation of Endometrium in Sterility Group

Day of M.C. tissue taken	No. of biopsies taken			Histological maturity of tissue					
				Mature			Immature		
	P.S.	S.S.	H.A.	P.S.	S.S.	H.A.	P.S.	S.S.	H.A.
*L.P. (8-14 days)	65	25	10	57	23	9	8	2	1
**L.S. (22 days+)	65	25	10	55	21	8	10	4	2

* Late proliferative
** Late secretory

(% calculated from total No. of biopsies taken in particular phase of cycle)

TABLE II

Distribution of Endometrial Glycogen in Different Phases of Menstrual Cycle in Primary Sterility Group

Histological Phase of Endometria	Amount of glycogen				
	—	+	++	+++	++++
* E.P. (73)	70 (95.89)	3 (4.11)	—	—	—
** L.P. (57)	6 (10.53)	36 (63.16)	15 (26.31)	—	—
*** E.S. (75)	12 (16.00)	14 (18.66)	13 (17.33)	25 (33.34)	11 (14.67)
**** L.S. (55)	2 (3.63)	3 (5.55)	20 (36.36)	24 (43.63)	6 (10.83)

* Early proliferative ** Late proliferative
*** Early secretory **** Late secretory

TABLE III

Distribution of Glycogen in Different Phases of Menstrual Cycle in Secondary Sterility Group

Histological Phase of Endometria	Amount of Glycogen				
	—	+	++	+++	++++
E.P. (29)	26 (93.11)	3 (6.89)	—	—	—
L.P. (21)	3 (14.28)	14 (66.66)	4 (19.06)	—	—
E.S. (28)	4 (14.28)	3 (10.72)	4 (14.28)	12 (42.85)	5 (17.87)
L.S. (22)	1 (4.55)	1 (4.55)	4 (18.18)	13 (59.09)	3 (13.63)

TABLE IV

Distribution of Glycogen in Different Phases of Menstrual Cycle in Habitual Abortion Group

Histological phase of Endometria	Amount of Glycogen				
	—	+	++	+++	++++
* E.P. (11)	9 (81.82)	2 (18.18)	—	—	—
** L.P. (9)	2 (22.22)	6 (66.67)	1 (11.11)	—	—
*** E.S. (12)	1 (8.33)	2 (16.67)	3 (25.00)	2 (16.67)	4 (33.33)
**** L.S. (8)	1 (12.50)	1 (12.50)	1 (12.50)	3 (37.50)	2 (25.0)

* Early proliferative ** Late proliferative
*** Early secretory **** Late secretory

Histochemical study of immature endometria showed glycopenia in all of them except one in which it was present in adequate amounts.

Histochemical study in proliferative endometria revealed no conclusive results as regards the cause of infertility. They contained glycogen either in traces or none at all. This small amount was because of immaturity or of its being in proliferative phase, could not be said with certainty and hence no inference could be drawn from such a study.

ation and intensity of histochemical reaction in control group and in cases of dysfunctional uterine haemorrhage associated with normal endometrium. Atrophic endometrium showed no glycogen at all, distribution of glycogen in mixed pattern endometria was variable corresponding to histological variation. The histochemical reaction varied from gland to gland in cystic glandular hyperplasia (Table V).

TABLE V

Distribution of Glycogen in Different Histological Patterns Encountered in Dysfunctional Uterine Haemorrhage Group

Different Histological Patterns	Amount of glycogen				
	—	+	++	+++	++++
E.P. (23) *	13	5	—	—	—
L.P. (22) **	5	13	4	—	—
E.S. (18) ***	—	—	2	9	7
L.S. (17) ****	—	2	12	3	—
M.H. (6) *****	2	2	1	1	—
Ad. H. (3) ******	1	1	1	—	—
Atrophic (5)	5	—	—	—	—
Mixed pattern (6)	—	—	4	2	—

* Early proliferative
** Late proliferative
*** Early secretory
**** Late secretory
***** Metropathia haemorrhagica
****** Adenomatous hyperplasia

Dysfunctional uterine haemorrhage group

Histological study

Out of 100 cases 60 showed normal endometrium, 6 cystic glandular hyperplasia, 6 hormonal imbalance (mixed pattern) 3 adenomatious hyperplasia and 5 atrophic endometrium.

Histochemistry

There was no difference seen in localis-

Discussion

In the present series histological immaturity in proliferative phase was found to be in 8.00% specimens of primary sterility, 2.00% of secondary sterility and 1.00% of habitual abortion group. Inadequate endometrium may in some way be responsible for secretory endometrium apparently presenting a normal histological picture but inadequate functionally. Baveja (1972) found 30% immature endometria in secretory phase in contrast to 15.55% in our series (primary sterility and secondary sterility group). In habi-

tual abortion group incidence of immature endometria in second half of menstrial cycle was 20% in contrast to 72.7% found by Baveja (1972).

In the present series glycogen deficiency in secretory phase was seen in 22.5% of specimens of sterility group. Zondek and Stein, 1940; Zondek and Shapino, 1942) found glycopenia in 18.4% of normal progestational endometria in cases of primary sterility. Hughes (1949, Shahani *et al* (1959) and Baveja (1972) also found glycogen deficiency in progestational endometria in cases of sterility. Shetty (1959) found glycogen deficiency in 44.6% of cases of sterility. Dass and Mookerjea (1964) could not find glycogen deficiency in any of their 10 cases of habitual abortion.

Zondek and Stein's glycopenic uteri (1940) and Hughes deficient endometrium (1950) both signify the importance of glycogen before and at the time of implantation. Deficiency of glycogen at the time of ovulation may result in deficient uterine secretion at the time of sperm migration and to an inadequate uterine bed at the time of implantation and hence may be one of the causes of infertility and early abortion. Whether the endometrium is primarily at fault or there is quantitative deficiency in the secretion of pituitary and ovarian hormones that control the metabolism is equally incertain. That quantitative biochemical estimations are more accurate and reliable than histochemical findings based on density and distribution of stainable material and that glycogen deficiency observed in one cycle does not hold good for other cycles also are important criticism against this approach. Besides this it is still believed that a good glycogen level in the progestational endometrium is always favourable for successful implantation.

Dysfunctional Uterine Haemorrhage Group

The results in the present series were more or less similar to those of Stuemer and Stein (1951), Dass and Mookerjea (1964) and Hinge and Solanki (1974). The histochemical study of glycogen in this group of cases did not show any specific alteration and hence could not help in the diagnosis of dysfunctional uterine bleeding which is purely a clinical syndrome. Correlation is not possible between clinical, histopathological and histochemical study.

Summary

Carbohydrate metabolism has been considered as essential for successful pregnancy. For this reason endometrial glycogen was studied in different phases of menstrual cycle in cases of infertility with a view to see if any significant histochemical changes occur in endometrium which may be responsible for sterility and habitual abortion. Histologically retarded endometria obtained in early proliferative phase may mature to secretory phase but may in some way be inadequate functionally. Study of glycogen in secretory endometria showed dificiency in 22.5% specimens. Glycogen study did not help in finding out the cause of dysfunctional uterine haemorrhage.

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